

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference AHB/FP6155089	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/08928	International filing date (day/month/year) 12.08.2003	Priority date (day/month/year) 14.08.2002
International Patent Classification (IPC) or both national classification and IPC C12N15/62		
Applicant AVIDIS SA ET AL.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
- This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I Basis of the opinion
 - II Priority
 - III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV Lack of unity of invention
 - V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI Certain documents cited
 - VII Certain defects in the international application
 - VIII Certain observations on the international application

Date of submission of the demand 12.03.2004	Date of completion of this report 08.07.2004
Name and mailing address of the International preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Devijver, K Telephone No. +31 70 340-4124



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/08928

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-56 as originally filed

Sequence listings part of the description, Pages

1-10 as originally filed

Claims, Numbers

1-21 as originally filed

Drawings, Sheets

19-99 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the International application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description; pages:
- the claims; Nos.:
- the drawings; sheets:

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5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-20
	No: Claims	21
Inventive step (IS)	Yes: Claims	
	No: Claims	1-21
Industrial applicability (IA)	Yes: Claims	1-15,18,19,21
	No: Claims	16,17,20

2. Citations and explanations

see separate sheet

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EXAMINATION REPORT - SEPARATE SHEET**

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Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. CITATIONS

Reference is made to the following documents:

- D1: WO 91 11461 A (BIOGEN INC) 8 August 1991 (1991-08-08) cited in the application
- D2: BLOM A M ET AL: 'The C4b-binding protein-protein S interaction is hydrophobic in nature' BIOCHIMICA ET BIOPHYSICA ACTA. PROTEIN STRUCTURE AND MOLECULAR ENZYMOLOGY, ELSEVIER, AMSTERDAM,, NL, vol. 1388, no. 1, 14 October 1998 (1998-10-14), pages 181-189, XP004278525 ISSN: 0167-4838

2. NOVELTY (Art. 33(2) PCT)

- 2.1 D1 discloses a eukaryotic expression vector comprising a nucleic acid sequence encoding a recombinant fusion protein comprising a scaffold of a C-terminal core protein of C4bp alpha chain for the use in the treatment of the human or animal body (cf. figures 7 and 9, claim 52 and description page 30 line 32 - page 31 line 13). Hence D1 anticipates the subject-matter of claim 21.
- 2.2 The present application does not satisfy the criterion set forth in Article 33(2) PCT, because the subject-matter of claim 21 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

3. INVENTIVE STEP (Art. 33(3) PCT)

- 3.1 The present application does not satisfy the criterion set forth in Article 33(3) PCT, because the subject-matter of claims 1-21 does not involve an inventive step in the sense of Article 33(3) PCT.
- 3.2 Document D1 is considered to represent the most relevant state of the art and

discloses a method for obtaining a recombinant fusion protein comprising a scaffold of a C-terminal core protein of C4bp alpha chain, said fusion protein being capable of forming multimers in soluble form, using a eukaryotic host cell (cf. examples 4-7, figures 7 and 9 and claims 1-67). The subject-matter of claim 1 differs in that a prokaryotic host cell is used.

- 3.3 The problem to be solved by the present invention may therefore be regarded as providing an alternative host cell for the expression of said fusion proteins. The proposed solution is that a prokaryotic host cell is used.
- 3.4 This solution cannot however be considered as involving an inventive step for the following reasons. Although there is no experimental demonstration, D1 suggests that prokaryotic host cells (e.g. Escherichia coli) may be used in the production of said fusion proteins (cf. description page 23 line 26 - page 25 line 32), so the person skilled in the art has a clear incentive to express said fusion proteins using a prokaryotic host cell and hence the present solution is obvious. Inventive step in this case can only be acknowledged if a prejudice, against the use of prokaryotic host cells, has been overcome by the present application and this prejudice should be substantiated for the specific proteins of the invention, not in general, because D2 already shows that a C4bp beta chain expressed in bacterial system (and thus lacking glycosylation) binds to protein S with the same affinity as the plasma purified protein (cf. page 182 paragraph 1). Therefore, the subject-matter of claim 1 does not appear to involve an inventive step in the sense of Art. 33(3) PCT.
- 3.5 Claims 2-21 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT with respect to inventive step (Art. 33(3) PCT), because they merely relate to straightforward biotechnological applications and products (nucleic acids, vectors, host cells, proteins) or alternatives (e.g. different heterologous polypeptides) which are well-known to the person skilled in the art (cf. D1 claims 1-15 (nucleic acids), 16-19 (host cells), 20-39 (proteins), description page 23 line 26 - page 24 line 23 (vectors) and page 17 lines 3-8 (heterologous polypeptides)).
- 3.6 Claim 4 merely states further E. coli strains, namely C41(DE3) [B96070444], C43(DE3) [96070445] and CO214(DE3) [NCIMB40884]. Lacking any unexpected effect linked to the use of said strains, this claim is considered to lack an inventive

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step.

4. FURTHER REMARKS

- 4.1 For the assessment of the present claims 16, 17 and 20 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
- 4.2 Claim 6 contains an obvious error, because it refers back to claims 1 to 6 while this should obviously be claims 1 to 5.
- 4.3 Claim 16 contains an obvious error, because it refers back to claim 14 while this should obviously be claim 13.